

REMARKS

Claims 19, 20, 23, 24, 29-31, 33, 34, 36, 38 and 40-43 are pending and stand ready for further action on the merits. Claims 19, 23, 24, 29-31, 33, 34 and 40 have been withdrawn from consideration as being drawn to non-elected subject matter.

Independent claims 19, 20 and 42 have been amended to recite that the IRES sequence is from a tobamovirus. In addition, claims 44-48 are newly cancelled herein.

No new matter has been added by way of the above amendments.

Interview

Applicants would like to thank Examiner Lambertson for his time and consideration with the telephone interview of September 15, 2004 with Applicants' representatives in the U.S. and Germany. The Applicants found the Examiner's comments very helpful in addressing the issues raised in the Office Action and each of the Examiner's concerns are addressed herein.

Sequence Listing

Applicants' note the Examiner's request that the figures be in a Sequence Listing. An appropriate Sequence Listing is being prepared and will be submitted under separate cover at a later date.

Restriction of the claims

The Examiner maintains the restriction requirement as between:

Group I - Process claims 19, 23, 24, 29-31, 33, 34, 40 and 44;

and

Group II - Product claims 20, 36, 38 and 41-43, 45-48.

Applicants respectfully request rejoinder of the withdrawn process claims as being drawn to a process for making a product that is both novel and unobvious. During the interview, the Examiner indicated that if rejoined, the process claims may be subject to rejections under 35 U.S.C. §112, 1st and/or 2nd paragraph.

However Applicants fully believe that the withdrawn process claims are fully compliant with the requirements for patentability under 35 U.S.C. §112, 1st and 2nd paragraphs. Regarding 35 U.S.C. §112, 2nd paragraph, the withdrawn process claims use the same language to describe the claimed features as do the elected claims which have been deemed definite. As such, the elements and features of the process claims are also definite for purposes of 35 U.S.C. §112, 2nd paragraph.

Regarding 35 U.S.C. §112, 1st paragraph, enablement, the specification provides working examples of transgenic plant and animal cell lines made in accordance to the process of independent claim 19. As such, Applicants are claiming no more than they have demonstrated with working examples and the invention is therefore fully enabled. Regarding 35 U.S.C. §112, 1st paragraph, written

description, Applicants are again claiming no more than is described in the specification. As discussed below, the specification fully describes the genus of IRES sequences from tobamoviruses such that one skilled in the art would view the present inventors to be in possession of the claimed genus at the time of the invention. In addition, the examples of the specification fully support transgenic plant and animal cell lines or clones transformed with the IRES sequences of the invention. As such, Applicants sufficiently described how to use the process encompassed by independent claim 19 and the dependent claims thereon so as to fulfill the requirements for written description. Rejoinder and allowance of the withdrawn claims are therefore respectfully requested.

Rejections under 35 U.S.C. §112, 1st paragraph, written description

Claims 20, 36, 38, 41-43 and 45-48 remain rejected under 35 U.S.C. §112, 1st paragraph for lack of written description. In support of the rejection, the Examiner asserts 1) that the specification contains no indication of structural requirements for IRES sequences of the invention, 2) that the specification discloses only a single IRES sequence and 3) that Ivanov et al. teach that the IRES sequence from crTMV is unique even to the genus of tobamoviruses. Applicants traverse this rejection and withdrawal thereof is respectfully requested.

Firstly, Applicants note that the present claims have been amended to be drawn to the genus of IRES sequences from tobamoviruses. The Examiner's assertions in forming the rejection are addressed in turn in relation to the amended claims.

The Examiner asserts that the specification discloses IRES sequences isolated from only a single species of tobamovirus, that being crTMV. The Examiner's assertion in this regard is incorrect because the specification discloses IRES sequences identified by the inventors in three different species of tobamovirus. On a related issue, Applicants note that the conclusion in Ivanov et al. that the IRES from crTMV is unique even to other tobamoviruses is incorrect. Attached hereto is a Declaration of the inventors submitted under 37 C.F.R. §1.132.

With the exception of Timo Korpela all of the present inventors were also authors on the Ivanov et al. article. As such, the inventors have first hand knowledge of the experiments, results and conclusions presented in Ivanov et al. As discussed in the Declaration, due to the experimental conditions used in the experiments of Ivanov et al., the authors/inventors were unable to detect an IRES sequence in TMV U1. In addition, the work in Ivanov et al. preceded the work reported in the present specification and had been submitted with a manuscript in August of 1996, i.e. prior to the Finnish priority date of the present application of May 30, 1997. Subsequent to the submission of the Ivanov et al. manuscript

the inventors determined that certain conclusions that had been reached in Ivanov et al. were, in fact, incorrect.

Specifically, subsequent to the submission of the Ivanov et al. paper, the authors/inventors determined with the experiments that led to the present application, that the failure to detect an IRES sequences in TMV U1 was an experimental artifact and IRES activity was detected for the sequence upstream of the coat protein gene of TMV U1 in yeast cells. It thus turned out that the conclusion of the Ivanov et al. reference that crTMV was unique in having IRES elements was incorrect. Indeed the specification reports the identification of IRES sequences in three different species of tobamovirus.

The genus of tobamovirus is a small one, with roughly 19 species. At the time of the invention approximately $\frac{1}{2}$ of those species had been identified, i.e. less than 10. Thus, the identification of the three IRES sequences in the specification is representative of the claimed genus. That the species disclosed in the specification adequately support the claimed genus is further supported by the common structural elements seen with all the IRES sequences from tobamoviruses.

In this regard, the Examiner asserts that the specification fails to disclose structural requirements for the IRES sequences of the invention. However, a review of the disclosure of the specification reveals that the IRES sequences do, in fact, have

common structural elements. For example, Figures 1B to 1H of the above-captioned application show predicted secondary structures of various tobamoviral IRESs. The 3'-end of the IRESs is defined by the AUG start codon. The RNA sequences forming these IRESs have pronounced self-complementarity, enabling the formation of multiple duplex (base-paired) structures in major parts of the IRES RNA sequences. Major parts of the IRESs are involved in secondary structures. The IRESs form at least one, and typically two to four stem-loops.

As can be further seen from the figures; the stems of the stem-loops can be very large, whereby large stems may be interrupted by bulges. These bulges frequently occur as symmetric bulge loops, i.e. the bulges occur on opposing strand segments and opposing bulges of a bulge loop frequently have the same number of bases. In addition, the primary structures of the IRESs share the common feature of being U-rich.

Coat protein IRESs are typically rich in purine bases in loops that connect stem-loops structures. Such purine-rich loops that connect stem-loop structures typically have more than four bases.

The skilled person envisions that tobamoviral IRESs other than those specifically mentioned and shown in Fig. 1B to 1H would have the same structural properties as described above under item 1 and, as a consequence, will also have IRES activity. As such, the claimed genus of IRES sequences from tobamoviruses for the present

invention is sufficiently described by the recognition of common structural features.

As the concerns raised by the Examiner have been addressed herein with the present amendments and corresponding remarks, withdrawal of the rejection is respectfully requested.

Rejection under 35 U.S.C. §112, 1st paragraph, Enablement

Claims 20, 36, 38, 41-43 and 45-48 remain rejected under 35 U.S.C. §112, 1st paragraph for lack of enablement. The Examiner has taken the position that the specification, while being enabling for an IRES of crTMV origin, does not reasonably provide enablement for any IRES of plant viral origin.

The Examiner maintains the rejection with the assertions that the claimed genus is broader than the enabled scope, that the specification discloses only a single IRES sequence from crTMV and that Ivanov et al. teach that the crTMV IRES sequence is unique even among other tobamoviruses. Applicants traverse this rejection and withdrawal thereof is respectfully requested.

With regard to the scope of the claims, the present invention has been amended to be defined as being IRES sequences from tobamoviruses. This genus is fully enabled by the specification. As discussed above, the specification discloses IRES sequences from three different tobamoviruses and all of the identified IRES sequences share common features, such that one skilled in the art

would conclude that IRES sequences could easily be isolated from other tobamoviruses using the same techniques as those disclosed in the specification. As further discussed above, the report in Ivanov et al. that the crTMV IRES sequence is unique even among tobamoviruses was erroneous and later found by the inventors to be an experimental artifact. As such, the present invention, as claimed, is fully enabled and withdrawal of the rejection is respectfully requested.

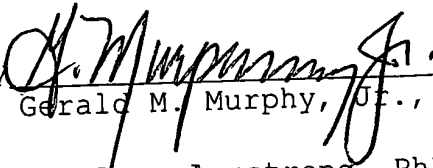
Attached hereto is another publication, Skulschev et al., Virology, Vol. 236 (1999) pp. 130-154, which the Examiner may want to make of record before allowing this application.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact MaryAnne Armstrong, PhD, (Reg. No. 40,069) at the telephone number of the undersigned below.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. §§ 1.16 or 1.17; particularly, extension of time fees.

Respectfully submitted,

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Attachment(s): 1) Declaration under 37 C.F.R. §1.132
 2) Skulschev et al., Virology, Vol. 236 (1999) pp. 130-154.